Translation

PCT/EP2003/008011

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

21 JAN 2005

| Applicant's or agent's file reference 28356P WO | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No. PCT/EP2003/008011 | International filing date (*day/month/year*) 22 July 2003 (22.07.2003) | Priority date (*day/month/year*) 24 July 2002 (24.07.2002) |
| International Patent Classification (IPC) or national classification and IPC A61K 31/495 | | |
| Applicant WILEX AG | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 19 September 2003 (19.09.2003) | 04 November 2004 (04.11.2004) |
| Name and mailing address of the IPEA/EP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/008011

## I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-29, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☒ the claims:

pages _____, as originally filed

pages _____, as amended (together with any statement under Article 19

pages _____, filed with the demand

pages 1-26, filed with the letter of 14 October 2004 (14.10.2004)

☒ the drawings:

pages 1/5-5/5, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 03/08011

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-26 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | 1-26 | YES |
| | Claims | | NO |
| Industrial applicability (IA) | Claims | 1-26 | YES |
| | Claims | | NO |

2. Citations and explanations

1. The documents are numbered according to the order in which they appear in the search report (D1 to D4). Unless otherwise indicated, reference is made to the passages from each document cited in the search report.

2. **Novelty (PCT Article 33(2))**

None of the cited documents discloses liposomal formulations with 3-amino- or 3-guanidino-phenylalanine derivatives in a weight proportion of 0.5 to 10%, based on the total weight of the formulation.

Therefore, the subject matter of claim 1 and of dependent claims 2-26 can be considered novel.

3. **Inventive Step (PCT Article 33(3))**

Document D1 relates to the use of 3-amidinophenyl-alanine derivatives, including the compound according to the present claim 2 (also known as WX UK1), for treating tumors and metastasis formation. These compounds can also be incorporated into the membranes of liposomes to make it possible to target the active substances (e.g. chemotherapeutics) enclosed in the liposomes (cf. page 14). The tests demonstrating the effectiveness of the substances are carried out with aqueous solutions.

The problem to be solved by the present application consists in reducing the undesirable side-effects (such as hemolysis and skin irritation) of aqueous solutions containing phenylalanine derivatives that are administered parenterally.

The solution proposed in the present application is that of providing 3-amino- or 3-guanidino-phenylalanine derivatives in liposomal formulations.

The applicant has demonstrated that liposomal formulations containing WX UK1 result in fewer skin irritations and a reduction in the hemolytic effect compared to aqueous solutions.

Therefore, the subject matter of claims 1-26 can be considered inventive.